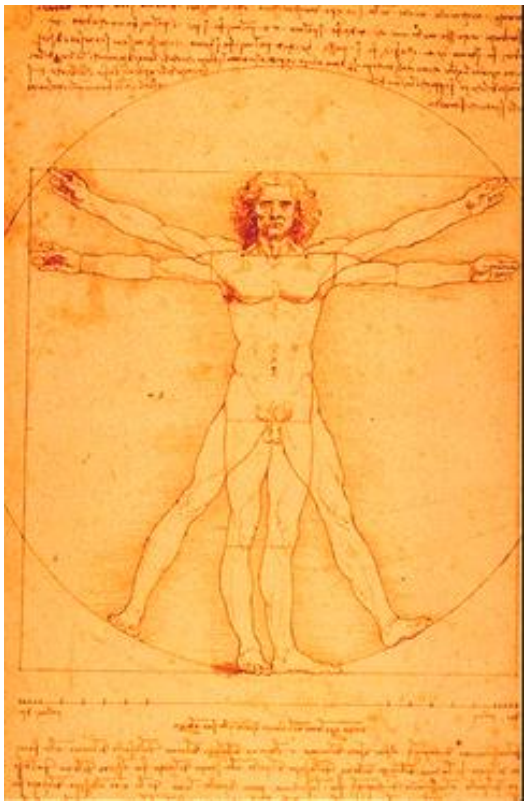
Phenomes

-- beyond genomes

Phenomes

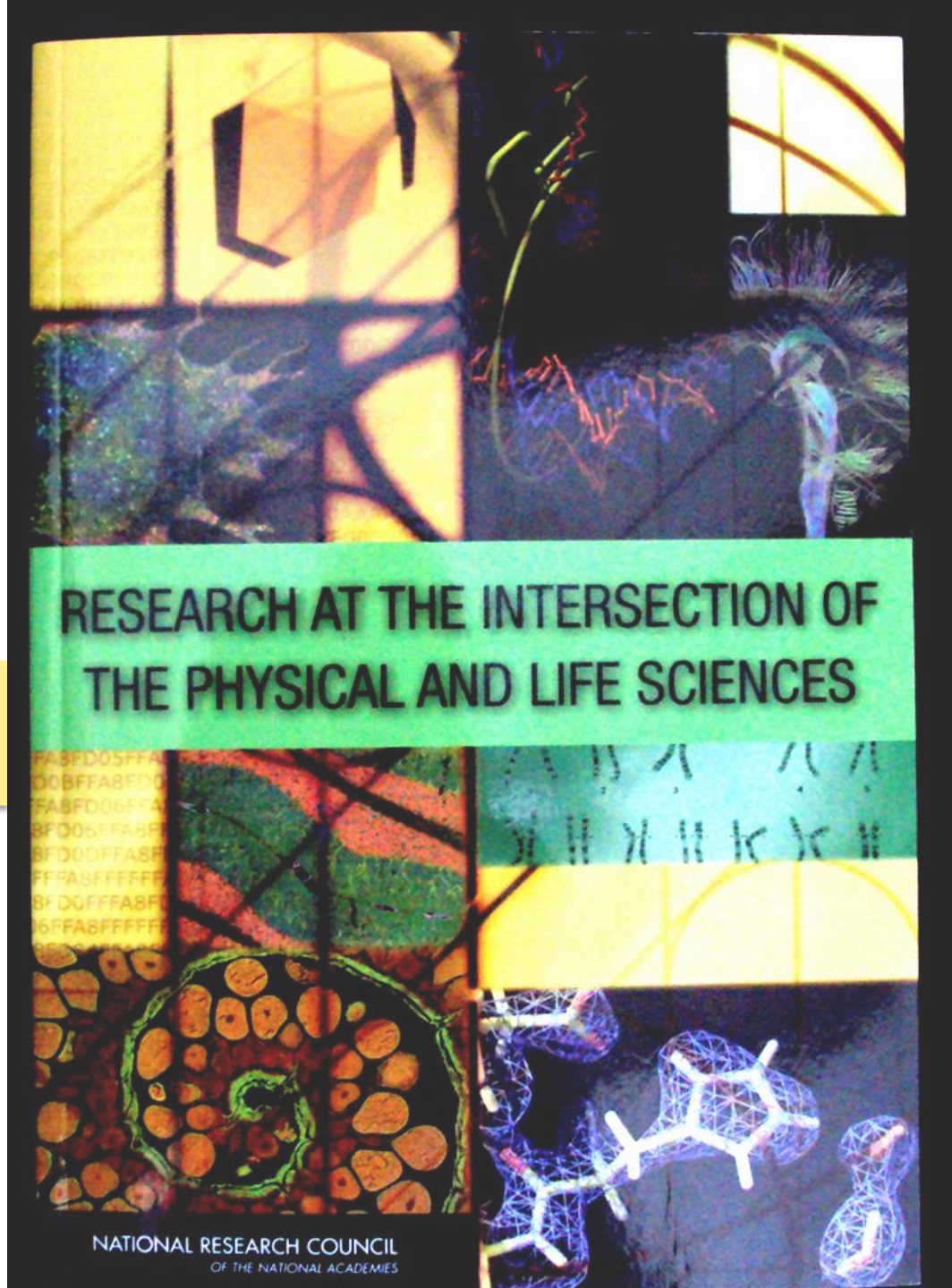


The genotype/phenotype problem

Second NRC Report

Grand Challenges

1) Synthesizing lifelike systems
2) Understanding the brain
3) Predicting phenotype from genotype
4) Earth, climate & biosphere interactions
5) Understanding biodiversity



Phenomes

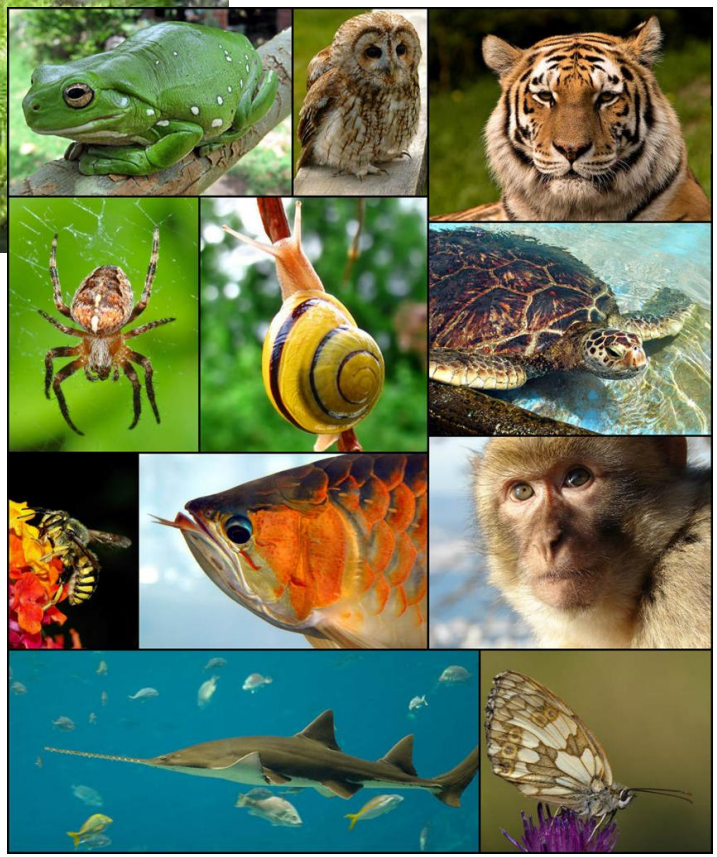
are about who and what we are

http://www.creationscience.com/onlinebook/webpictures/faces.jpg

Phenomes

http://www.condorjourneys-adventures.com/images/costarica_tabaconhotsprings.jpg

http://media-files.gather.com/images/d987/d981/d745/d224/d96/f3/full.jpg



http://upload.wikimedia.org/wikipedia/commons/c/cd/Animal_diversity_October_2007.jpg

are about biodiversity

Phenomes

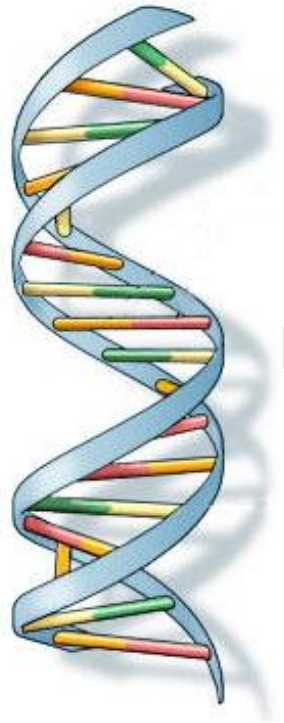
are about how organisms are shaped by and adapt to their environment

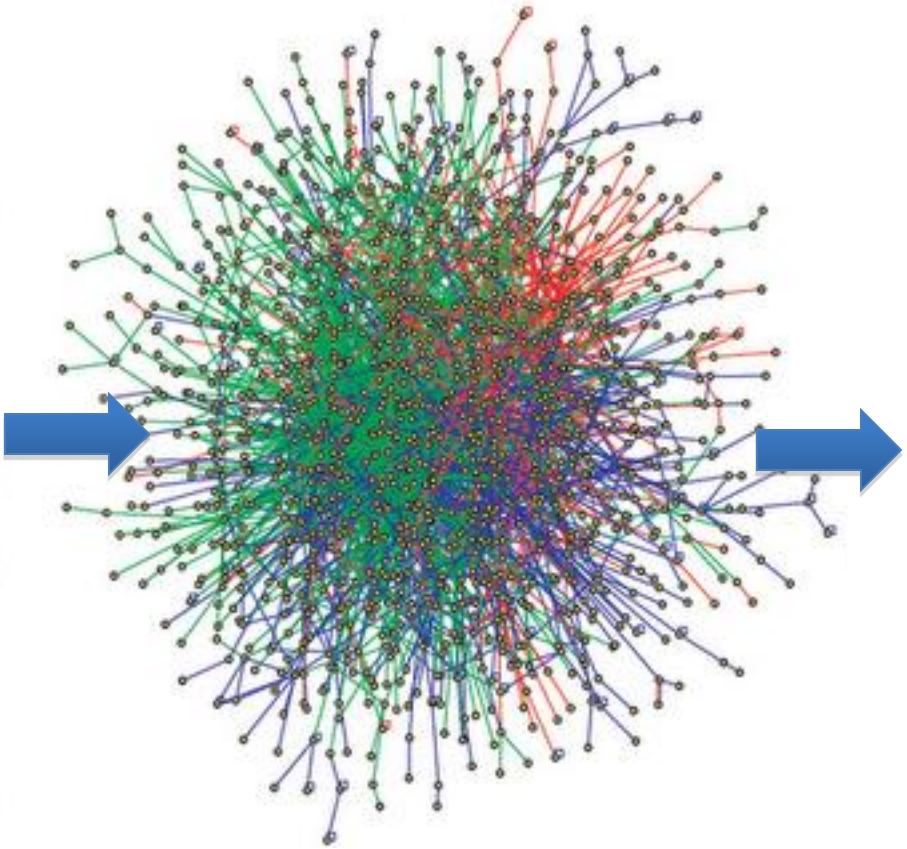
Phenomes

are about traits of organisms important to our environment and economy

http://www.theepochtimes.com/news_images/2005-7-6-51404533.jpg

The genotype/phenotype problem

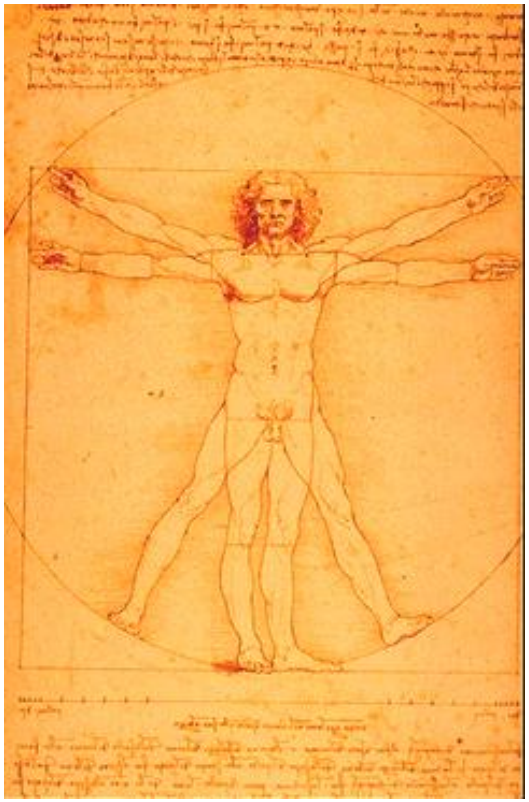




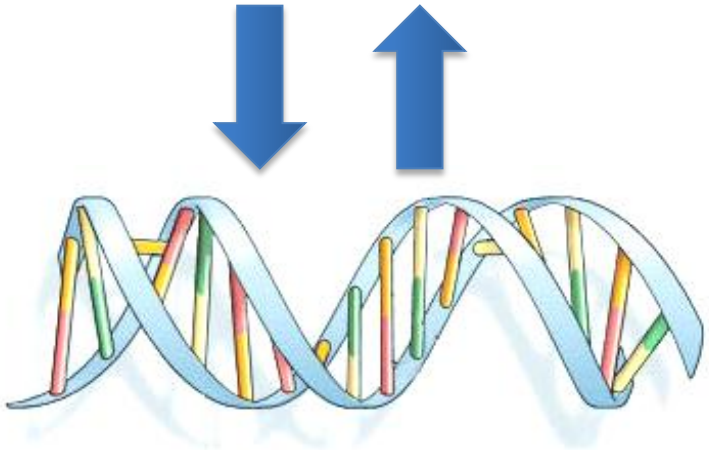
Genomes **Systems biology** **Hi-throughput phenotyping**

Top down approach

What do variants in the phenome tell us about the underlying genome?

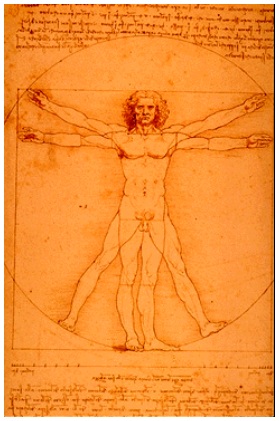


Can we predict the phenome from the underlying genome?

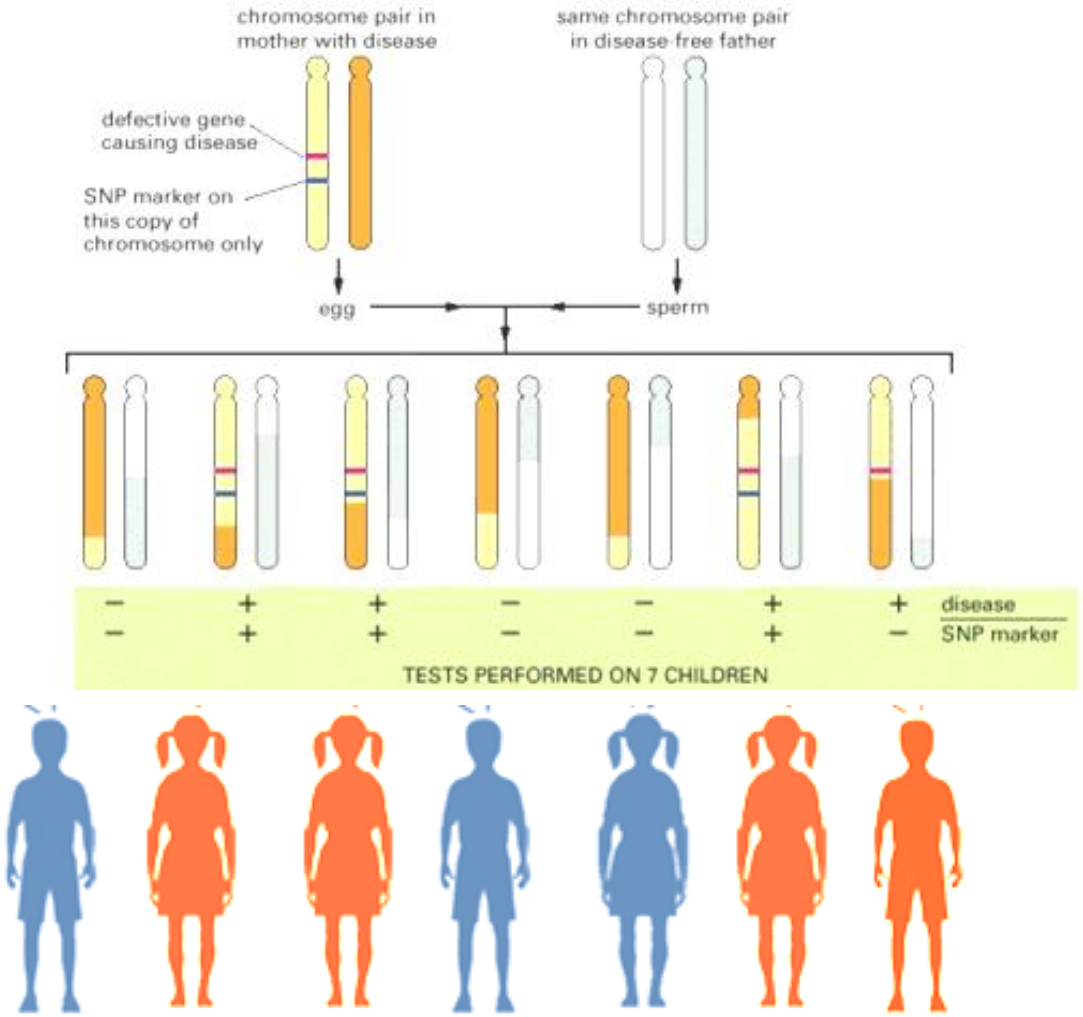


Bottom up approach

Top down approach

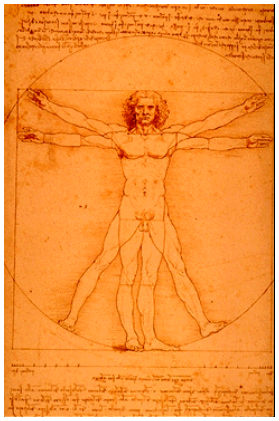


Linkage mapping

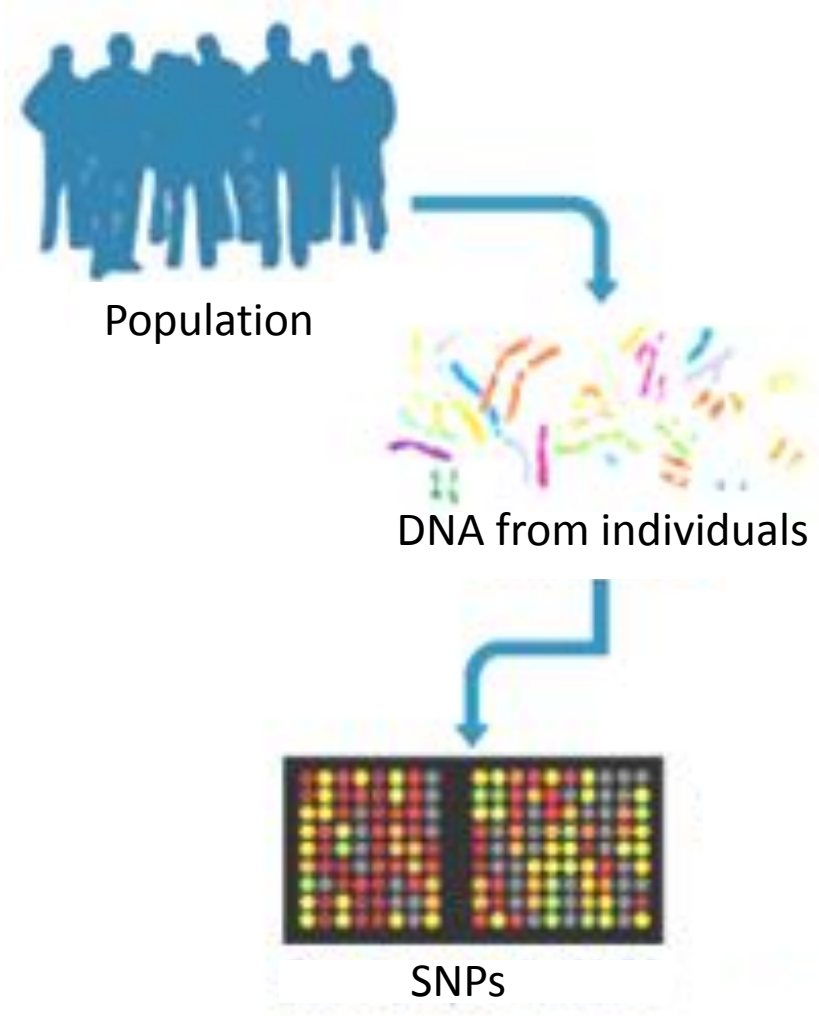


http://www.ncbi.nlm.nih.gov/ bookshelf/picrender.fcgi

Top down approach

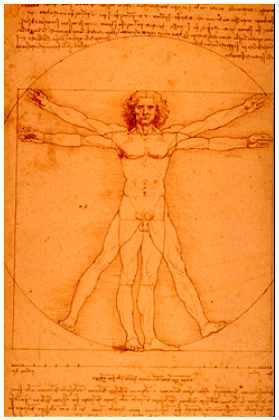


Genome-wide Association Studies (GWAS)



http://plan2009.cancer.gov/images/genome.jpg

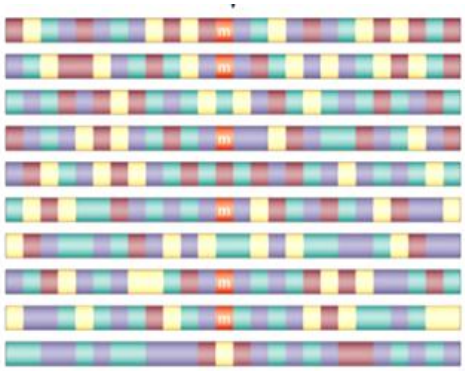
Top down approach

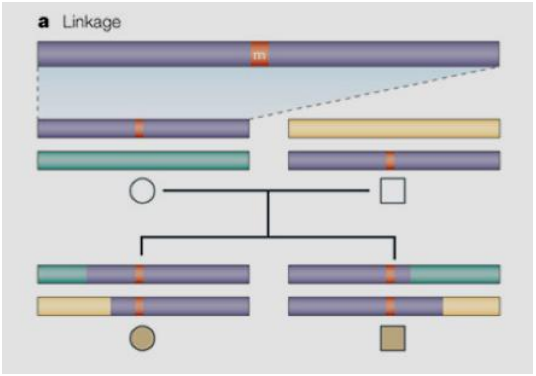


Nested Association Mapping (NAM) Population

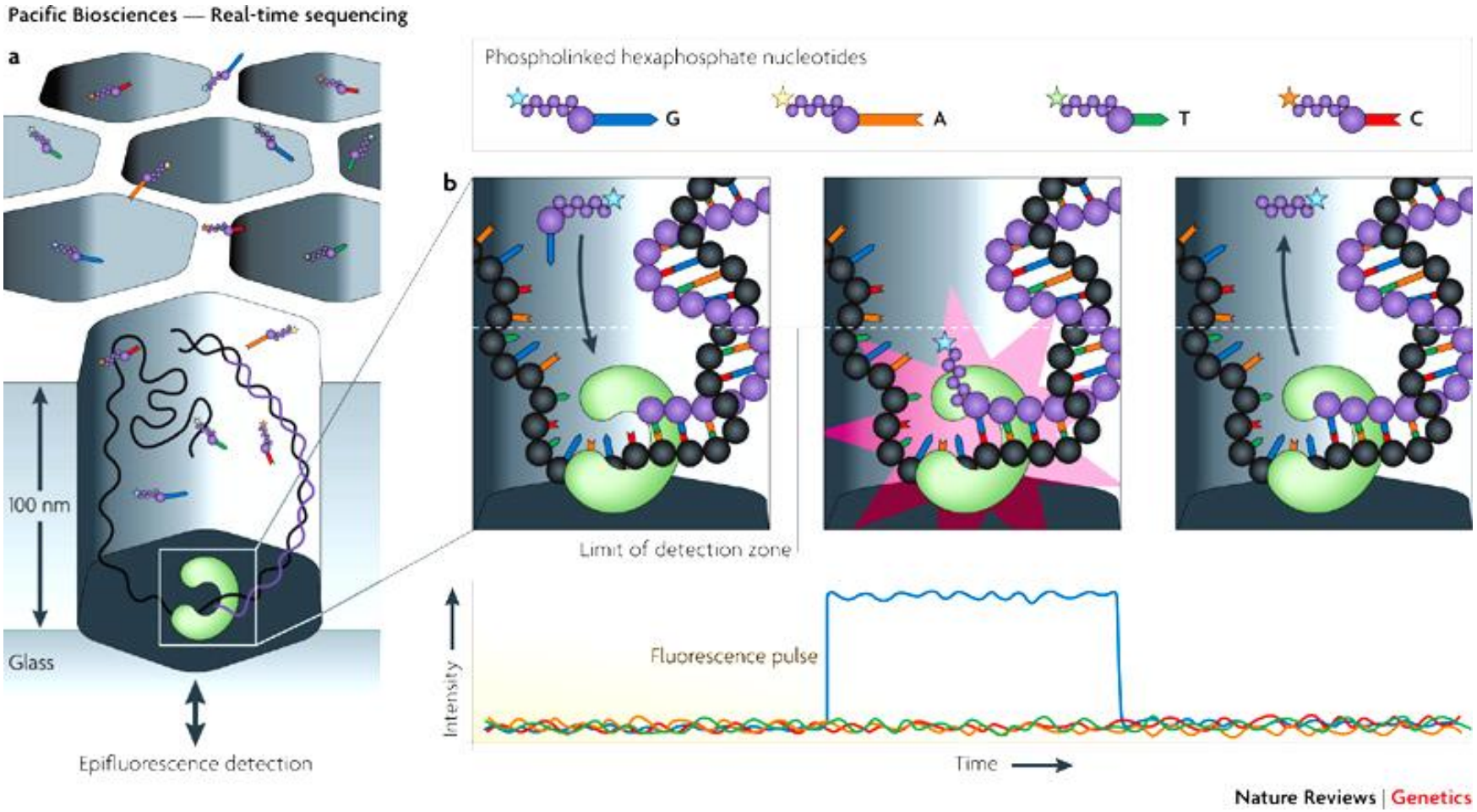
Ed Buckler

https://parmesan.mc.vanderbilt.edu/turnersd/ggd/2010-02-04-locuszoom-apoe.png

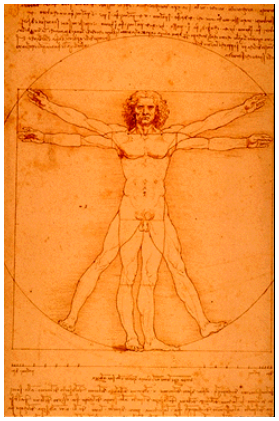




Real Time DNA Sequencing



Top down approach



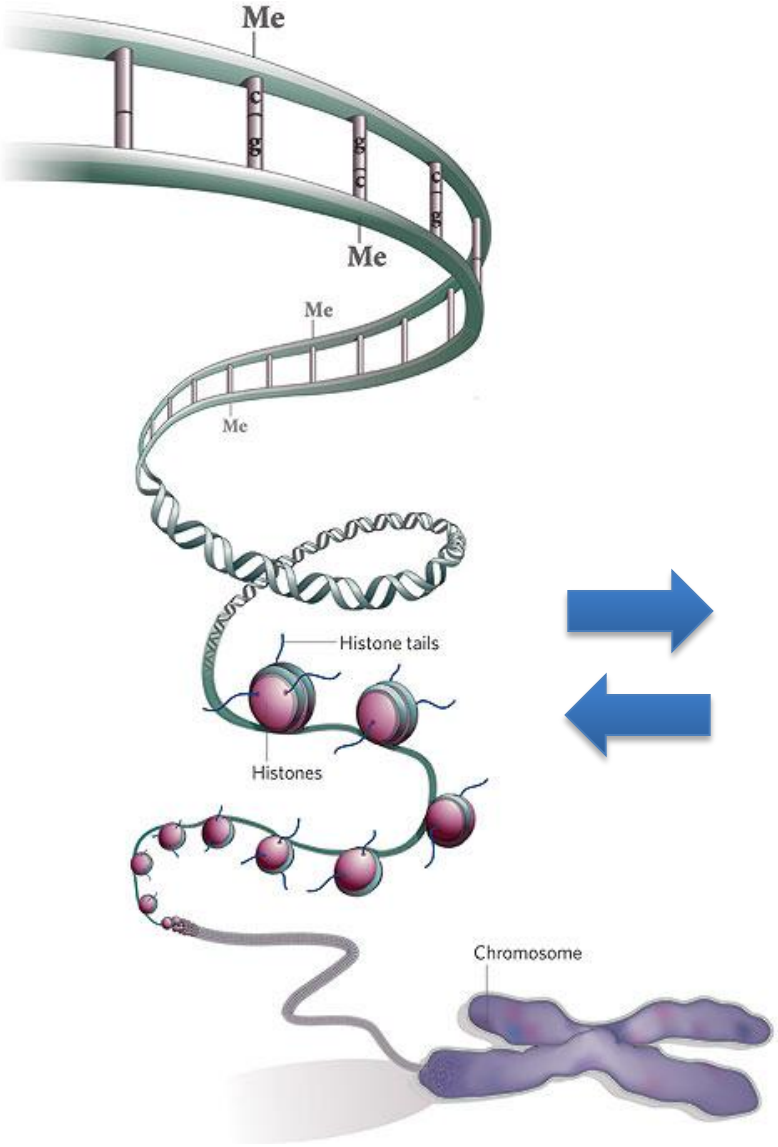
Phenome deconstruction

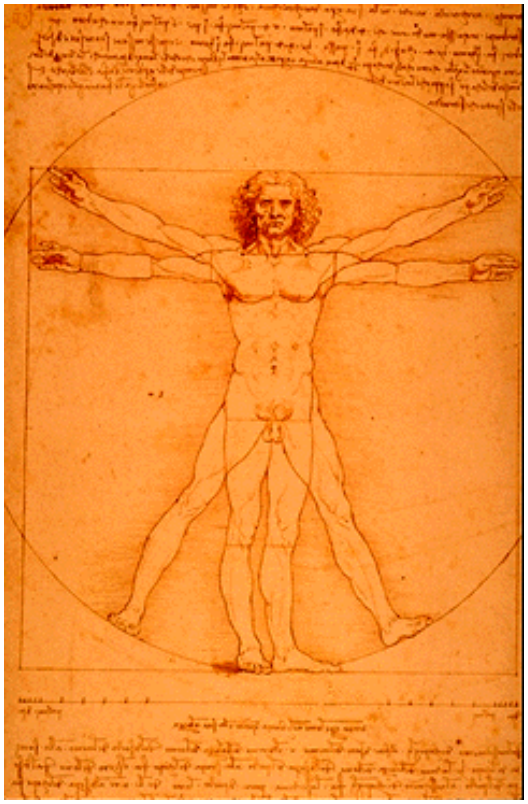
Association mapping

Susceptibility of lodgepole pine to mountain pine beetle

http://www.logcabindirectory.com/images/lodgepole-pine-courtesy-of-nfs.jpg

Epigenome

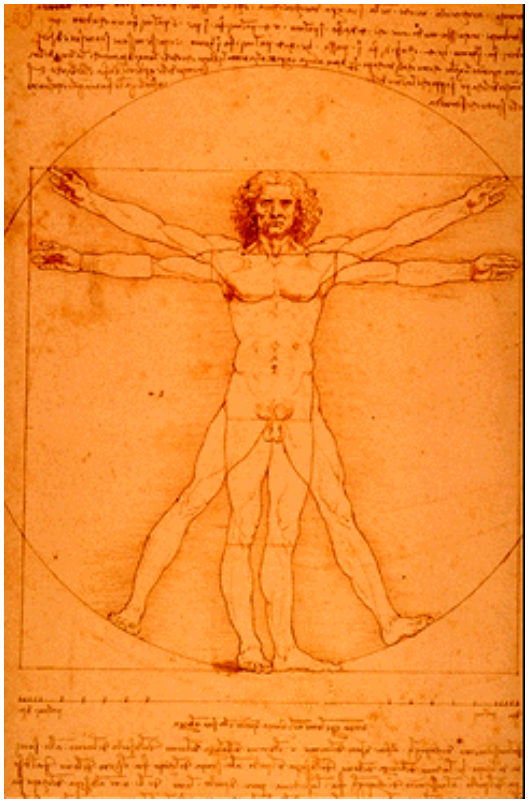




http://embryology.med.unsw.edu.au/MolDev/Images/epigenetics.jpg

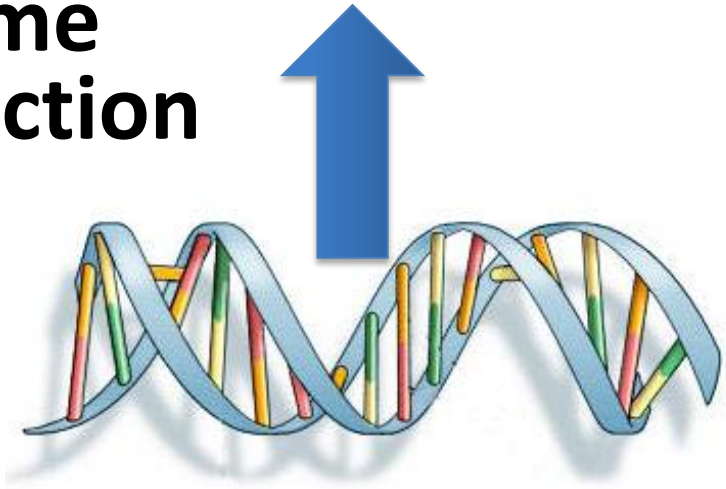
The epigenotype/phenotype problem

Bottom up approach

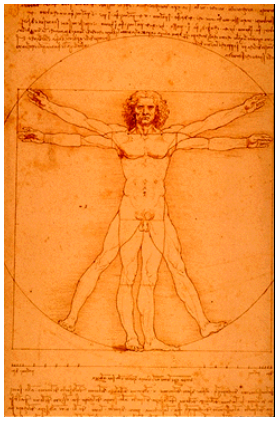


Can we predict the phenome from the underlying genome?

Phenome reconstruction

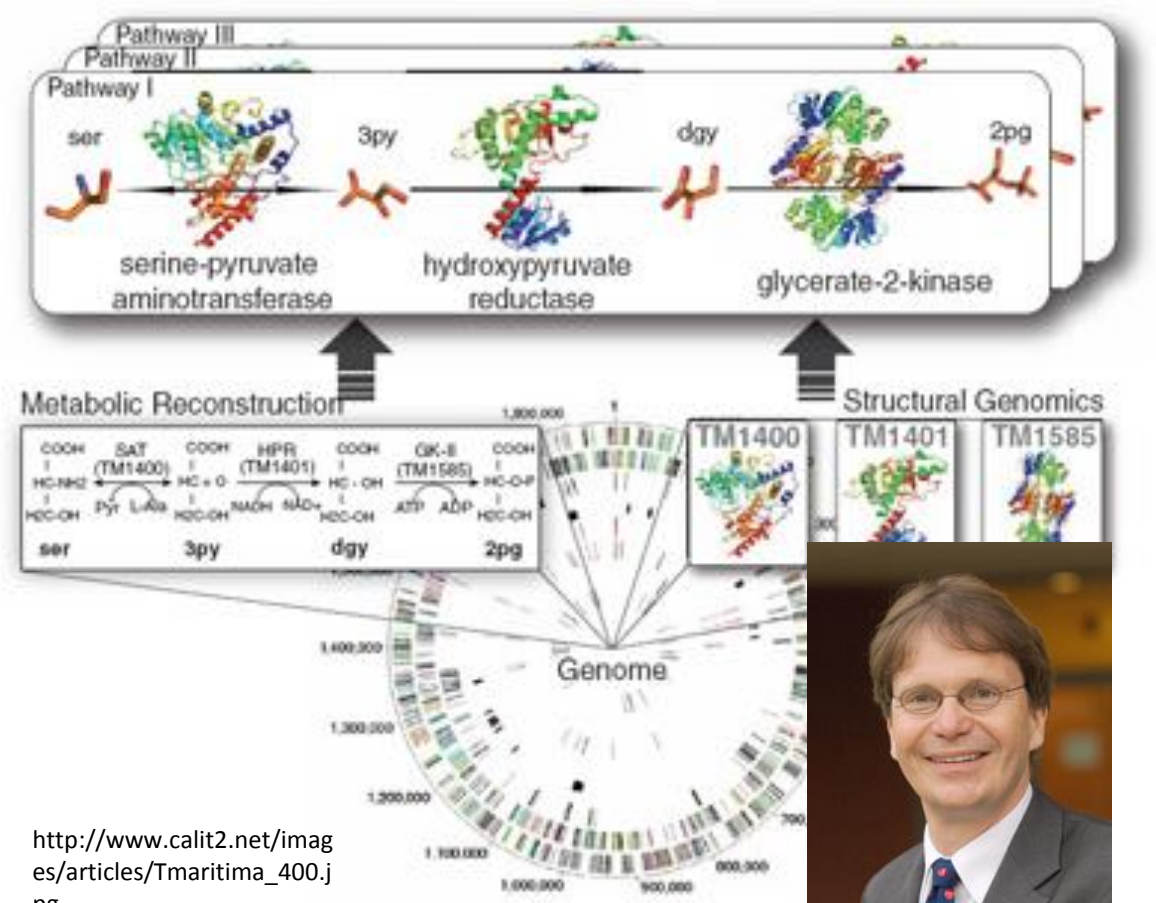


Bottom up approach



Phenome reconstruction

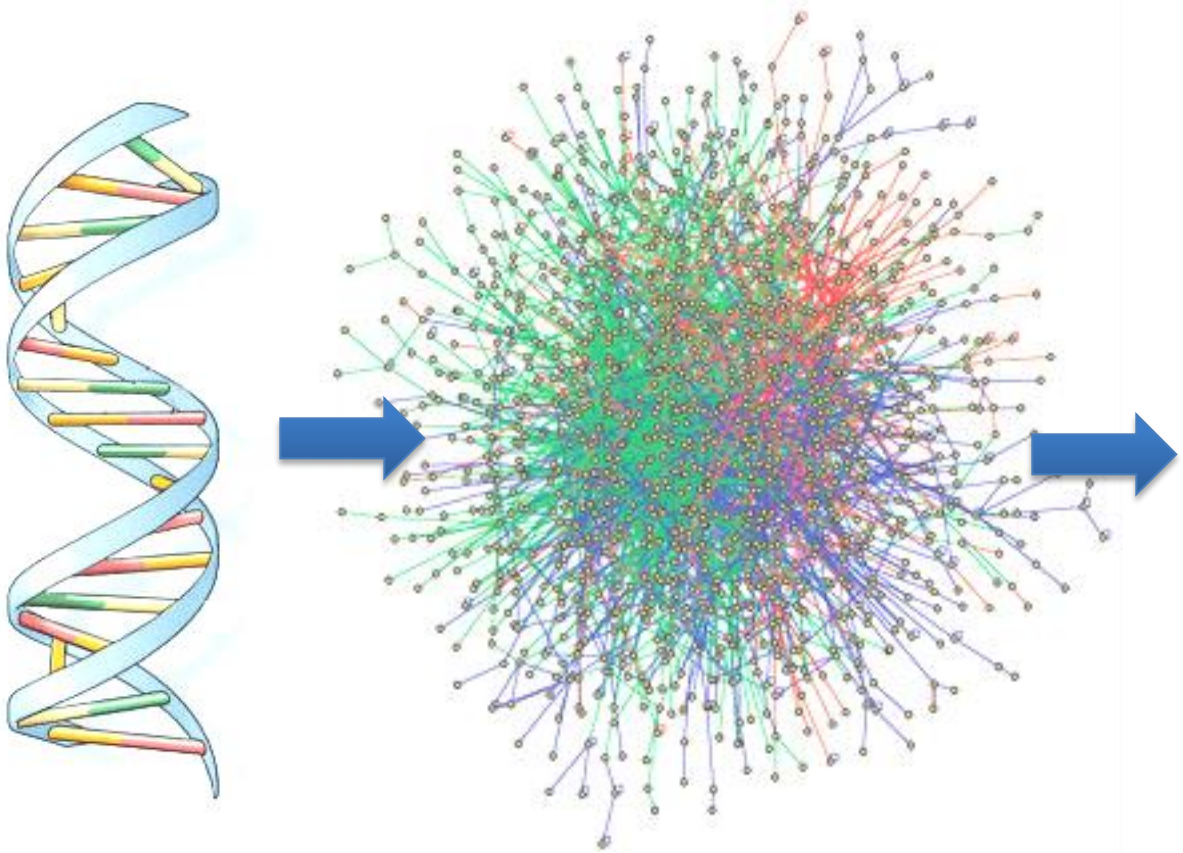
Metabolic reconstruction



http://www.calit2.net/images/articles/Tmaritima_400.jpg

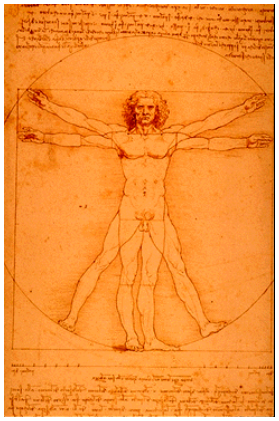
Bernhard Palsson

Predicting phenotype



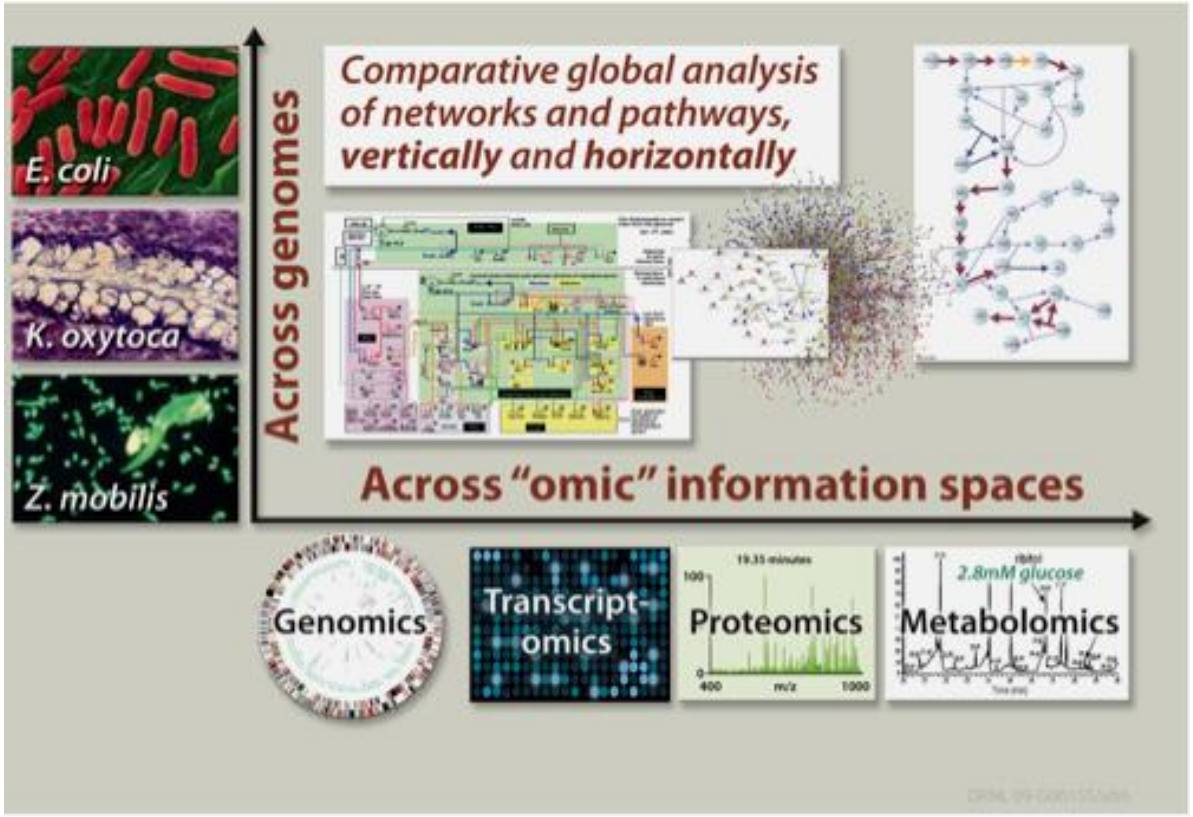
Systems biology

Bottom up approach

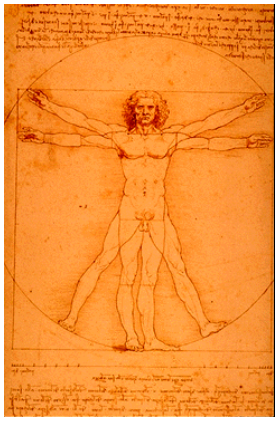


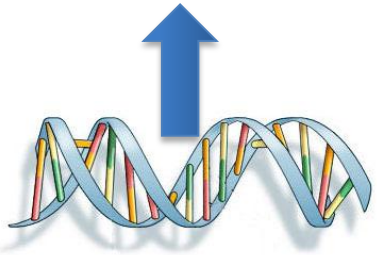
Phenome reconstruction

Integration of information



Bottom up approach



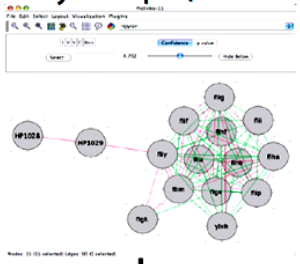


Phenome reconstruction

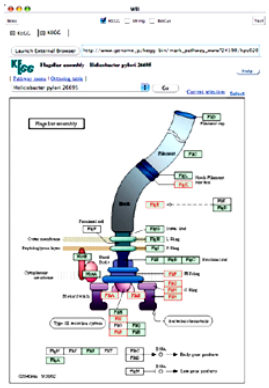
Tools for integration of information

Nitan Baliga

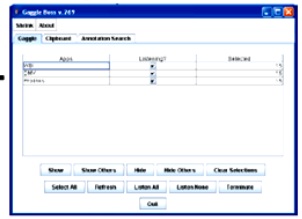
A. Cytoscape (Associations/interactions)



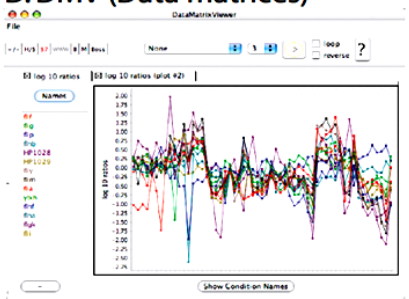
C. KEGG (Pathways)



B. Gaggle Boss

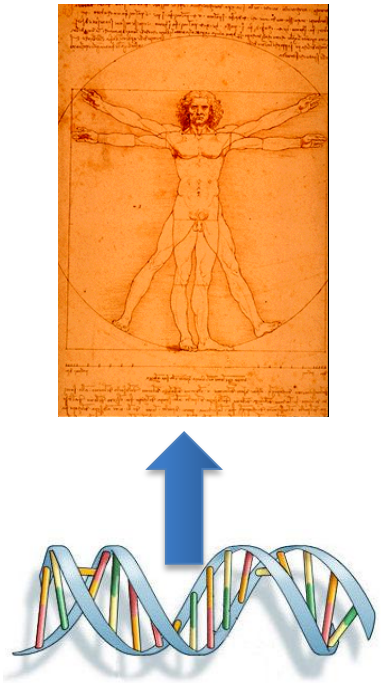


D. DMV (Data matrices)



(http://gaggle.systemsbiology.org) (Shannon et al., 2006)

Bottom up approach



Unknown genes

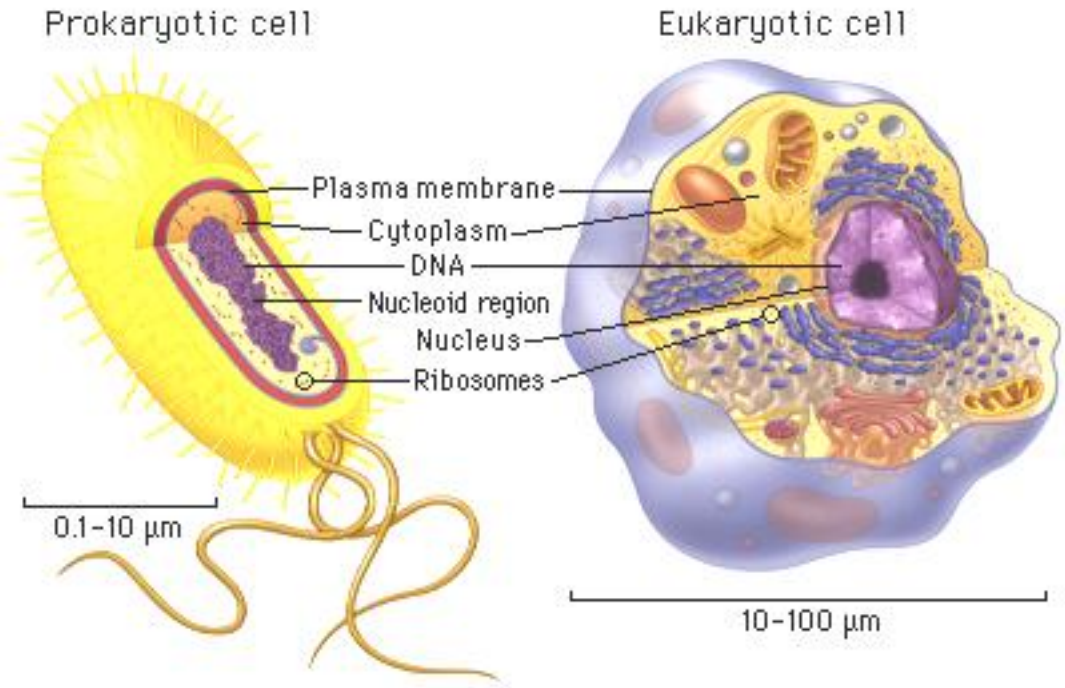
30-40% of the genes encoded by bacterial organisms have no know function (Osterman and Overbeek, 2003). Hanson et al (2010) estimate that with nearly 1000 bacterial genomes sequenced and with about 3000 genes per genome, that some 10^6 proteins are unknown. Genes without known function, of course, create gaps in metabolic pathways and in, some cases, leave out whole pathways from metabolic reconstructions.

Complexity in reconstructions

Complexity is added to reconstructions when they become conditional based on environmental conditions, particularly under stress. It might seem that organisms would have in their repertoire an infinite number of states in response to environmental conditions, but fortunately they do not. The observation has been made in *E. coli*, for example, that although the metabolic and transcriptional network involves some 1000 genes, they are organized to a achieve a few dominant modes of operation under a wide variety of conditions (Barrett et al., 2005).

http://wat.tldsb.on.ca/multisites/wat/images/stories/weather_icon.jpg

Complexity in reconstructions

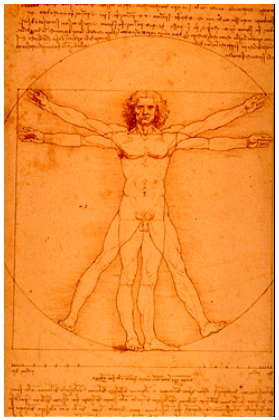


http://www.nslc.wustl.edu/courses/Bio2960/labs/04Organelle/allcell.jpg

Further complexity is involved in eucaryotic cells as compared to procaryotes, specifically when different tissues are involved in a multicellular organism.

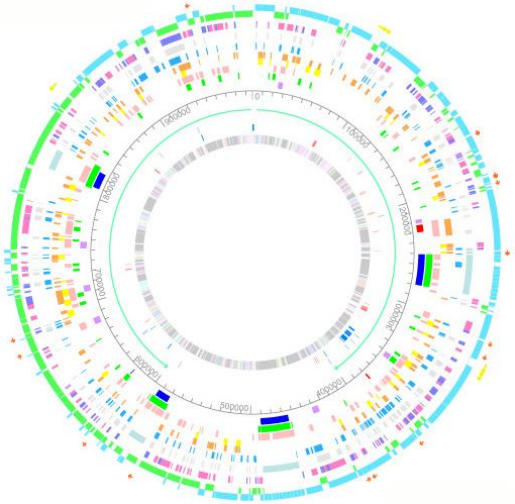
Even at the single cell level, metabolic reconstruction networks in procaryotes typically include 600 metabolites, 650 genes, and 800 reactions, whereas metabolic reconstruction of eucaryotes involve on average 1200 metabolites, 1000 genes, and 1500 reactions (Oberhardt et al., 2009).

Bottom up approach

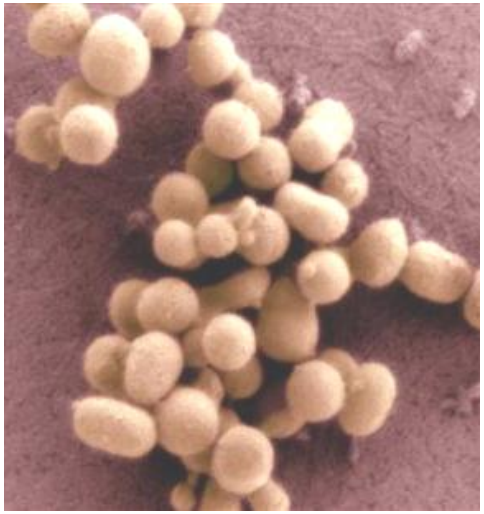


Reconstructions and synthetic biology

Phenotype reconstructions and systems biology are the foundation for synthetic biology. Reconstructions use *in silico* methods to reconstruct and simulate biological events, whereas synthetic biology attempts to create systems in the laboratory.



http://cevr.uconn.edu/MGRlowGenomeMap.jpg



http://in.reuters.com/news/pictures

Phenomes

The genotype/phenotype problem is huge. How should we draw boundaries around the problem to make it more tractable?